SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbox 100 mg/ml solution for injection for cattle and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Marbofloxacin 100.0 mg

Excipients:

Qualitative composition of excipients and other constituents
Glucono-delta-lactone.
Water for injections.

Clear yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs (sows).

3.2 Indications for use for each target species

Cattle:
Therapeutic treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica* and *Histophilus somni*.
Therapeutic treatment of acute mastitis caused by *E. coli* strains sensitive to marbofloxacin during the lactation period.

Sows:
Treatment of Metritis Mastitis Agalactia Syndrome caused by bacterial strains sensitive to marbofloxacin.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or other (fluoro)quinolones or to any of the excipients.
Do not use in case of confirmed or suspected resistance to fluoroquinolones (cross resistance).

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species
Use of the veterinary medicinal product should be based on susceptibility testing and has to take into account official and local antimicrobial policies.
It is prudent to reserve the fluoroquinolones for the treatment of clinical conditions that have responded poorly, or are expected to respond poorly, to other classes of antibiotics.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
People with known hypersensitivity to (fluoro)quinolones should avoid any contact with the veterinary medicinal product.
If the veterinary medicinal product comes into contact with the skin or eyes, rinse with copious amounts of water.
Take care to avoid accidental self-injection since it can induce a slight irritation.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the physician.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle:

Undetermined frequency	Injection site pain[1,3], Injection site inflammation[1,2], Injection site fibrosis[1,2], Injection site oedema[3]

[1] After intramuscular injection. Transient.
[2] Slight. The process of cicatrisation starts rapidly (varying from fibrosis to synthesis of extracellular matrice and collagen) and may persist for at least 15 days after injection.
[3] After subcutaneous injection. Slight to moderate.

Pigs (sows):

Undetermined frequency	Injection site oedema[1], Injection site inflammation[2]

[1] Very transient, slight
[2] Mild, persisting for 12 days after injection.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Laboratory studies in rats and rabbits have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effect.
Safety of the veterinary medicinal product at 2 mg/kg has been shown in cows during gestation and in suckling pigs and calves when used in sows and cows.
Safety of the veterinary medicinal product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle:
Intramuscular use:
- *Respiratory infections:*
8 mg marbofloxacin/kg bodyweight i.e. 2 ml of solution/25 kg bodyweight in a single injection.
If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

Subcutaneous use:
- *Acute mastitis:*
2 mg marbofloxacin/kg i.e. 1 ml of solution/50 kg bodyweight in a single daily injection, for 3 days.
The first injection may also be given by the intravenous route too.

Sows:
Intramuscular use:
2 mg marbofloxacin/kg i.e.1 ml of solution/50kg bodyweight in a single daily injection by intramuscular route, for 3 days.

To ensure a correct dosage body weight should be determined as accurately as possible.
As the vial cannot be broached more than 45 times, the user should choose the most appropriate vial size according to the target species to treat.
For the injections, the neck should be preferred in cattle and pigs.

3.10 Symptoms of overdose (and where applicable, emergency procedures, and antidotes)

No sign of overdosage has been observed in cattle after administration of 3 times the recommended dose.
Overdosage may cause signs such as acute neurological disorders which should be treated symptomatically.

3.11. Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Cattle:
Intramuscular: Meat and offal: 3 days - Milk : 72 hours.
Subcutaneous**:** Meat and offal: 6 days - Milk: 36 hours.

Sows:
Intramuscular: Meat and offal: 4 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01MA93

4.2 Pharmacodynamics

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group, which acts by inhibition of DNA gyrase. It has a broad-spectrum activity *in vitro* against Gram-negative bacteria (*Pasteurella multocida*, *Mannheimia haemolytica*, *Histophilus somni*, *E. coli*) and against Gram-positive bacteria (in particular *Staphylococcus)*.
Resistance to *Streptococcus* may occur.

Strains with MIC ≤ 1 µg/ml are sensitive to marbofloxacin whereas strains with MIC > 2 µg/ml are resistant to marbofloxacin.

Resistance to fluoroquinolones occurs by chromosomal mutation with three mechanisms: decrease of the bacterial wall permeability, expression of efflux pump or mutation of enzymes responsible for molecule binding.

4.3 Pharmacokinetics

Cattle- Intramuscular route
After a single intramuscular administration at the recommended dose of 8 mg/kg, the maximum plasma concentration of marbofloxacin (Cmax) is 8 µg/ml reached in approximatively 1 hour (Tmax). Marbofloxacin is eliminated slowly (terminal T1/2 = 9.5 h), predominantly in the active form in urine and faeces.

Cattle- Subcutaneous route
After subcutaneous administration at the recommended dose of 2 mg/kg, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.7 µg/ml in approximately 1 hour. The terminal elimination half-life ($t_{½}$) of marbofloxacin is 5.6 hours.

Pigs- Intramuscular route
After intramuscular administration at the recommended dose of 2 mg/kg, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.7 µg/ml in approximately 1 hour. The terminal elimination half-life ($t_{½}$) of marbofloxacin is 8.7 hours.

Its bioavailability is close to 100 %.
Marbofloxacin is weakly bound to plasma proteins (less than 10% in pigs and 30 % in cattle), extensively distributed and in most tissues (liver, kidney, skin, lung, bladder, uterus) it achieves higher concentrations than in plasma.
Marbofloxacin is eliminated predominantly in the active form in urine and faeces.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Keep the container in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Primary packaging:
Amber PP/Ethylene vinyl alcohol/PP multi-layer plastic vials.
Type I chlorobutyl rubber stopper
Aluminium and plastic flip capsule.

Pack size
Cardboard box containing one 50 ml vial
Cardboard box containing one 100 ml vial
Cardboard box containing one 250 ml vial
Cardboard box containing one 500 ml vial

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorization: {DD/MM/YYYY}

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary/*).

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard boxes of 50, 100, 250 and 500 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbox 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 100 mg of marbofloxacin

3. PACKAGE SIZE

50 ml
100 ml
250 ml
500 ml

4. TARGET SPECIES

Catte and pigs (sows)

5. INDICATION(S)

6. ROUTES OF ADMINISTRATION

Cattle: intramuscular, subcutaneous or intravenous
Pigs: intramuscular

7. WITHDRAWAL PERIODS

Withdrawal periods
Cattle:
Intramuscular: Meat and offal: 3 days - Milk: 72 hours
Subcutaneous**:** Meat and offal: 6 days - Milk: 36 hours
Sows:
Intramuscular: Meat and offal: 4 days

8. EXPIRY DATE

Exp.
Once opened, use within 28 days by: ___/___/___

9. SPECIAL STORAGE PRECAUTIONS

Keep the container in the outer carton in order to protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

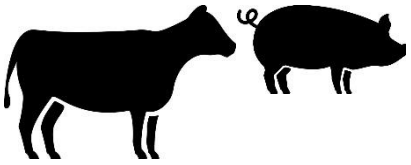
Lot:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial label of 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbox



2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S)

100 mg of marbofloxacin per ml

3. BATCH NUMBER

Lot:

4. EXPIRY DATE

Exp;
Once opened, use within 28 days by: ___/___/___

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vial labels of 100, 250 and 500 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbox 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 100 mg of marbofloxacin

3. TARGET SPECIES

Cattle and pigs (sows)

4. ROUTES OF ADMINISTRATION

Cattle: IM, SC or IV
Sows: IM.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:
Cattle:
IM: Meat and offal: 3 days - Milk: 72 hours
SC**:** Meat and offal: 6 days - Milk: 36 hours

Sows:
IM: Meat and offal: 4 days

6. EXPIRY DATE

Exp.
Once opened, use within 28 days, by: ___/___/___

7. SPECIAL STORAGE PRECAUTIONS

Keep the container in the outer carton in order to protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot:

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Marbox 100 mg/ml solution for injection for cattle and pigs

2. Composition

Each ml contains:

Active substance:
Marbofloxacin .....100.0 mg

Clear, yellow solution.

3. Target species

Cattle and pigs (sows)

4. Indications for use

Cattle:
Therapeutic treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica* and *Histophilus somni*.
Therapeutic treatment of acute mastitis caused by *E. coli* strains sensitive to marbofloxacin during the lactation period.

Sows:
Treatment of Metritis Mastitis Agalactiae Syndrome caused by bacterial strains sensitive to marbofloxacin.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or other (fuoro)quinolones or to any of the excipients.
Do not use in case of confirmed or suspected resistance to fluoroquinolones (cross resistance).

6. Special warnings

Special precautions for safe use in the target species:
The use of the veterinary medicinal product should be based on susceptibility testing and has to take into account official and local antimicrobial policies.
It is prudent to reserve the fluoroquinolones for the treatment of clinical conditions that have responded poorly, or are expected to respond poorly, to other classes of antibiotics.
The use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to (fluoro)quinolones should avoid any contact with the veterinary medicinal product.
If the veterinary medicinal product comes into contact with the skin or eyes, rinse with copious amounts of water.
Take care to avoid accidental self-injection since it can induce a slight irritation.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the physician.
Wash hands after use.

Pregnancy and lactation:
Laboratory studies in rats and rabbits have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effect.
The safety of the veterinary medicinal product at 2 mg/kg has been shown in cows during gestation and in suckling pigs and calves when used in sows and cows.
The safety of the veterinary medicinal product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows. Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
No sign of overdosage has been observed in cattle after administration of 3 times the recommended dose.
Overdosage may cause signs such as acute neurological disorders which should be treated symptomatically.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Cattle:

Undetermined frequency
Injection site pain[1,3], Injection site inflammation[1,2], Injection site fibrosis[1,2] (scarring), Injection site oedema[3] (swelling)

[1] After intramuscular injection. Transient
[2]Slight. The process of cicatrisation starts rapidly (varying from fibrosis to synthesis of extracellular matrice and collagen) and may persist for at least 15 days after injection.
[3] After subcutaneous injection. Slight to moderate.

Pigs (sows):

Undetermined frequency
Injection site oedema[1], Injection site inflammation[2]

[1] Very transient, slight.
[2] Mild, persisting for 12 days after injection.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian.

You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Cattle:
Intramuscular use:
- *Respiratory infections:*
8 mg marbofloxacin/kg bodyweight i.e. 2 ml of solution/25 kg bodyweight in a single injection.
If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

Subcutaneous use:
- *Acute mastitis:*
2 mg marbofloxacin/kg i.e. 1 ml of solution/50 kg bodyweight in a single daily injection, for 3 days.
The first injection may also be given by the intravenous route too.

Sows:
Intramuscular use:
2 mg marbofloxacin/kg i.e.1 ml of solution/50kg bodyweight in a single daily injection by intramuscular route, for 3 days.

9. Advice on correct administration

To ensure a correct dosage, body weight should be determined as accurately as possible.
As the vial cannot be broached more than 45 times, the user should choose the most appropriate vial size according to the target species to treat.
For the injections, the neck should be preferred in cattle and pigs.

10. Withdrawal periods

Cattle:
Intramuscular: Meat and offal: 3 days - Milk : 72 hours
Subcutaneous**:** Meat and offal: 6 days - Milk: 36 hours

Sows:
Intramuscular: Meat and offal: 4 days

11. Special storage precautions

Keep out of the sight and reach of children.
Keep the container in the outer carton in order to protect from light.
Do not use after the expiry date stated on the carton and vial after EXP. The expiry date refers to the last day of that month.
Shelf-life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

MA: xxxxxxxxx
Pack size:
Cardboard box containing one 50 ml vial
Cardboard box containing one 100 ml vial
Cardboard box containing one 250 ml vial
Cardboard box containing one 500 ml vial

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database *https://medicines.health.europa.eu/veterinary*

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Tel: +800 35 22 11 51
E-mail: pharmacovigilance@ceva.com

Local representatives and contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Ceva Santé Animale, 10, av. de La Ballastière, 33500 Libourne, France.

17. Other information